REMARKS

Reconsideration of this application is respectfully requested.

Claims 7, 27, and 28 have been canceled. Claims 8-12 have been amended.

Upon amendment, claims 6, 8-12, and 25-26 are pending in the application. Support for amended claims 8-12 can be found throughout the specification, for example, in original claims 8-12.

Applicants have also amended the specification at page 4, line 14 and page 15, line 7 to replace "∀-helices" with "α-helices." Support for this amendment can be found in the reference entitled Skouloubris et al. at page 4520 in the legend to Figure 3 (*Infection and Immunity*; 66(9): 4517-4521 (1998)). Skouloubris et al. is incorporated into the specification at page 15, line 27, was submitted to the Office, and was initialed by the Examiner on the PTO Form 1449 in the Office Action mailed April 27, 2004. Figure 3 of Skouloubris et al. reports the same graphic as shown at Figures 3(A) and 3(B) of this application, and indicates that the boxed regions show predicted transmembrane α-helices. Applicants further submit that one of skill in the art would recognize that α-helices denote a common and well characterized protein domain, whereas ∀-helices likely arose from a typographical error. A courtesy copy of the Skouloubris et al. reference is provided at Tab B.

Applicants submit that these amendments are fully supported by the specification, do not introduce new matter or require a further search of the art, and respectfully request their entry.

Priority

The Office contends that Applicants have failed to comply with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120. (Office Action at item 1.) In part, the Office contends that the first sentence of the specification contains errors in the filing dates of Application Serial Nos. 09/742,361 and 09/107,383. Applicants have amended the first sentence of the specification to contain the correct filing dates.

The Office also contends that the issue date for U.S. Patent No. 5,190,667 should be set forth in the first sentence of the Specification. In an effort to facilitate prosecution, Applicants have amended the first sentence to set forth the issue date.

The Office also asserts that PCT/EP99/04490 does not claim priority to U.S. Application No. 09/107,383, and therefore is not a Continuation-in-Part of U.S. Application No. 09/107,383. (Office Action at item 1d.) Applicants respectfully traverse. As proof that the stated priority claim is correct, Applicants direct the Office's attention to the Priority Data and Related Application Data listed on the cover page of WO 00/00634, the International Publication of Application No. PCT/EP99/04490 (attached at Tab A). Applicants respectfully submit (1) that the Priority Data for PCT/EP99/04490 lists U.S Application No. 09/107,383, and (2) that PCT/EP99/04490 is Related by Continuation-in-Part to U.S. Application Serial No. 09/107,383.

Given the correction of the filing dates, the inclusion of the issue date, and the evidence that the stated priority claim is correct, Applicants respectfully request the benefit of an earlier filing date under 35 U.S.C. § 120.

Drawings

The Office objected to drawings 3A and 3B because the Brief Description of the Drawings did not refer to each of the frames shown in the figures. (Office Action at Item 3.) Applicants have Amended the Brief Description of the Drawings to refer to both Figure 3A and to Figure 3B, and respectfully request withdrawal of this objection.

Claim Rejections under 35 U.S.C. § 102

Labigne et al. (U.S. Patent No. 6,258,359)

The Office rejected claims 6-7, 9-11, and 25-27 under 35 U.S.C. § 102(e) as being anticipated by Labigne et al. (U.S. Patent No. 6,258,359). (Office Action at item 5.) In particular, the Office alleges that Labigne et al. disclose a method of treating *H. pylori* infection through formulating UreI polypeptide into a composition to induce antibodies that interfere with the activation process of the urease apoenzyme, wherein the antibodies are induced *in vivo* in man or animal. (Office Action at item 5.) Claims 7 and 27 have been canceled, so the rejection of these claims is now moot. Applicants respectfully traverse the rejection of claim 6, amended claims 9-11, and amended claims 25 and 26.

Labigne et al. state that antibodies raised against UreI gene product preferentially are capable of interfering "with the activation process of the urease apoenzyme." (Labigne et al., col. 10, ll. 24-27.) Labigne et al. also state that antibodies "may be used in therapeutic treatment of *Helicobacter pylori* infection in man by blocking the urease maturation process." (Labigne et al., col. 11, ll. 30-32.) However, the UreI deficient *H. pylori* strain used in the method of the instant invention is urease

positive, and thus is not identified by its capacity to block the urease maturation process.

Applicants further point out that in order to properly establish that Labigne et al. anticipates Applicants' claimed invention under 35 U.S.C. § 102(e), each and every element of the claim in issue must be found, either expressly described or under principles of inherency, in that single reference. Furthermore, "[t]he identical invention must be shown in as complete detail as is contained in the . . . claim." *See* M.P.E.P. §2131, 8th Ed., Aug. 2001, p. 2100-69, quoting *Richardson v. Suzuki Motor Co.*, 868 F.2d 1126, 1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989). Finally, "[t]he elements must be arranged as required by the claim." M.P.E.P. §2131, p. 2100-69. Regarding the 35 U.S.C. § 102(e) rejection, Labigne et al. does not teach each and every element of Applicants' present invention as claimed.

Claim 6 recites, among other things, "testing and comparing the response to extracellular pH and the sensitivity to acidity of the parental strain to a strain deficient in UreI and/or of a UreI deficient strain complemented with a plasmid carrying *ureI* in the presence or absence of said active molecule." Labigne et al. nowhere discloses testing and comparing the response to extracellular pH and the sensitivity to acidity. Further, Labigne et al. nowhere discloses the selective use of UreI parental and deficient strains. Because Labigne does not teach each and every element of claim 6, Labigne et al. cannot anticipate claim 6, or dependent claims 9-11, 25, and 26.

Labigne et al. further fails to teach elements of dependent claims 9-11, 25, and 26. For example, claim 9 recites a molecule that inactivates UreI by inhibiting its properties in *H. pylori* resistance to acidity. Labigne et al. does not disclose whether or

not UreI antibodies affect the resistance to acidity of *H. pylori*. Claim 10 recites a molecule that inactivates UreI by inhibiting its property as a transporter. Labigne et al. does not address whether or not its antibodies inhibit the transport properties of UreI. Claim 11 recites a molecule that inactivates UreI "by inhibiting an interaction between UreI and other *H. pylori* proteins." Labigne et al. does not disclose whether or not UreI antibodies inhibit an interaction between UreI and other *H. pylori* proteins. Claim 26 recites a molecule that "specifically inhibits UreI transporter properties either in ammonia export or in urea export or import. Labigne et al. does not address whether or not UreI antibodies specifically inhibit UreI transporter properties in ammonia export or in urea export or import. Because Labigne does not teach each and every element of claims 9-11, 25, and 26, Labigne et al. cannot anticipate these claims.

Iversen et al. (U.S. Patent No. 6,124,271)

The Office rejected claims 6-7, 12, and 28 under 35 U.S.C. § 102(e) as being anticipated by Iversen et al. (U.S. Patent No. 6,124,271). (Office Action at item 6.) In particular, the Office alleges that Iversen discloses administering *H. pylori* urease oligomer. Applicants have canceled claims 7 and 28, thus, the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to claim 6 and amended claim 12.

Claim 6 recites treating or preventing *H. pylori* infection with a molecule displaying a differential effect on parental and UreI deficient strains. Iversen et al. does not teach a molecule for treating *H. pylori* infection based on displaying a differential effect on parental and UreI deficient strains. A claim is anticipated only if each and

every element as set forth in the claim is found in a single prior art reference. M.P.E.P. § 2131.01 Because Iversen et al. does not teach selecting a molecule displaying a differential effect on parental and Urel deficient strains, it cannot anticipate claim 6 or dependent claim 12.

Nakazawa et al. (U.S. Patent No. 5,214,053)

The Office rejected claims 6-11 and 25-28 under 35 U.S.C. § 102(b) as being anticipated by Nakazawa et al. (U.S. Patent No. 5,214,053). (Office Action at items 7-8.) In particular, the Office alleged that Nakawaza et al. inherently anticipates the claimed invention, as Nakazawa et al. discloses thiourea compositions that have antimicrobial activity against *H. pylori*. (Office Action at item 8.) Applicants have canceled claims 7, 27, and 28, so the rejection of these claims is now moot. Applicants respectfully traverse with respect to claims 6, 8-11, 25, and 26.

As stated above, claim 6 recites treating or preventing *H. pylori* infection with a molecule displaying a differential effect on parental and Urel deficient strains. Nakazawa et al. does not teach the use of a molecule displaying a differential effect on parental and Urel deficient strains, and thus cannot anticipate claim 6. Claim 6 also recites comparing the response to extracellular pH and the sensitivity to acidity of a parental strain and a Urel deficient strain, which also is not disclosed in Nakazawa et al.

The Federal Circuit has explained that "[u]nder the doctrine of inherency, if an element is not expressly disclosed in a prior art reference, the reference will still be deemed to anticipate a subsequent claim if the missing element is necessarily present in the thing described in the reference, and that it would be so recognized by persons of

ordinary skill." *Rosco Inc v. Mirror Lite Co.*, 64 U.S.P.Q.2d 1676, 1680 (Fed. Cir. 2002) (emphasis added). Applicants submit that the thiourea compositions of Nakazawa et al. need not necessarily show differential effect in sensitivity to acidity between a parental *Helicobacter* and a strain deficient in UreI, as there is no teaching in Nakazawa et al. as to which subunit of the urease enzyme is disrupted by the thiourea compositions. Accordingly, the rejection of claim 6, as well as dependent claims 8-11 and 25-26, is improper.

Hartmann (U.S. Patent No. 5,900,410)

The Office also rejected claims 6-11 and 27 under 35 U.S.C. § 102(b) as being anticipated by Hartmann (U.S. Patent No. 5,900,410) as evidenced by Nawaz et al. (1994). (Office Action at item 9.) In particular, the Office contends that Hartmann discloses a method of treating *H. pylori* infection by administering a divalent cation of Mg, an antibiotic, and urea together with a pharmaceutically acceptable carrier. The Office alleges that Hartmann inherently anticipates the instantly claimed invention, as Nawaz et al. provides evidence that aliphatic amidases (such as UreI) are inhibited by divalent cations. (Office Action at item 9.) Applicants have cancelled claims 7 and 27, so the rejection is now moot with respect to these claims. Applicants respectfully traverse with respect to claims 6 and 8-11.

Nawaz et al. shows that Mg cation partially inhibits a purified aliphatic amidase from a *Rhodococcus* species. From this disclosure, the Office concludes that the administration of divalent cations in Hartmann can be used to treat infections of *H. pylori*. Applicants respectfully point out that "[i]nherency may not be established by

probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency." *Scaltech, Inc. v. Retec/Tetra, L.L.C.*, 51 U.S.P.Q.2d 1055, 1059 (Fed. Cir. 1999). Applicants submit that the Office has improperly concluded that Mg cation can be used to treat or prevent *H. pylori* infections in humans, as neither Hartmann et al. nor Nawaz et al. provide any indication of the *in vivo* effect of Mg cation on *H. pylori* Urel.

Applicants further submit that neither Hartman et al. nor Nawaz et al. provide any evidence that Mg divalent cation displays a differential effect on parental and Urel deficient strains, as is recited in claim 6. Under 35 U.S.C. § 102(b), each and every element of the claim in issue must be found, either expressly described or under principles of inherency, in that single reference. M.P.E.P. § 2131. Because neither Hartmann et al. nor Nawaz et al. explicitly or implicitly teach every element of claim 6, they cannot anticipate claim 6. Accordingly, the rejection of claim 6, as well as dependent claims 8-11 and 25-26, is improper.

WO 97/26908

The Office also rejected claims 6-7 under 35 U.S.C. § 102(a) as being anticipated by WO 97/26908. (Office Action at item 10.) In particular, the Office alleges that WO 97/26908 discloses a method of treating *Helicobacter pylori* infection comprising thiocyanate, as Gregoriou et al. provides evidence that thiocyanate is an inhibitor of amidase activity. (Office action at item 10.) Applicants respectfully traverse.

Gregoriou et al. shows that sodium cyanate inhibits purified amidase from *Pseudomonas aeurginosa* strain AI3. (Gregoriou et al., abstract.) From this disclosure,

the Office concludes that the thiocyanate in WO 97/26908 can be used to treat *H. pylori* infection. Applicants submit that the Office has improperly concluded that thiocyanate can be used to treat or prevent *H. pylori* infections in humans, as neither Hartmann et al. nor Nawaz et al. provide any indication of the *in vivo* effect of thiocyanate on *H. pylori* Urel.

Applicants further submit that neither WO97/26908 nor Gregorious et al. provide any evidence that thiocyanate displays a differential effect on parental and Urel deficient strains, as is recited in claim 6. Under 35 U.S.C. § 102(b), each and every element of the claim in issue must be found, either expressly described or under principles of inherency, in that single reference. M.P.E.P. § 2131. Because neither WO97/26908 nor Gregorious et al. explicitly or implicitly teach every element of claim 6, they cannot anticipate claim 6. Accordingly, the rejection of claim 6 is improper.

Zopf (U.S. Patent No. 5,514,660)

The Office asserts that claims 6 and 7 are rejected under 35 U.S.C. § 102(b) as being anticipated by Zopf (U.S. Patent No. 5,514,660) as evidenced by Gregoriou et al. (1979). In particular, the Office alleges that Zopf discloses a method of treating *H. pylori* infections by administering a cyanate derivative together with other antiulcerative compounds (see claims 10-11). Claim 7 has been canceled, so the rejection of this claim is now moot. Applicants respectfully traverse with respect to claim 6.

As stated above, claim 6 recites treating or preventing *H. pylori* infection with a molecule displaying a differential effect on parental and Urel deficient strains. Because

Zopf et al. does not teach a molecule displaying a differential effect on parental and UreI deficient strains, it cannot anticipate claim 6. *See* M.P.E.P. § 2131.01

Furthermore, as stated previously, Gregoriou et al. shows that sodium cyanate inhibits purified amidase from *Pseudomonas aeurginosa* strain AI3. (Gregoriou et al., abstract.) From this, the Office concludes that a cyanate derivative can be administered *in vivo* to inhibit *H. pylori* UreI. Applicants respectfully point out that "[i]nherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency." *Scaltech, Inc. v. Retec/Tetra, L.L.C.*, 51 U.S.P.Q.2d 1055, 1059 (Fed. Cir. 1999). Accordingly, Applicants respectfully submit that the rejection of claim 6 under Zopf et al. is improper.

In view of the foregoing amendments and remarks, Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. § 102.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: July 23, 2004

By: _____

Kenneth J. Meyers
Reg. No. 25,146
Phone: (202) 408-4000
Fax: (202) 408-4400
E-mail: ken.meyers@finnegan.com

Attachments:

Cover page of PCT International Publication No. WO 00/00634
Skouloubris et al. *Infection and Immunity*; 66(9): 4517-4521 (1998)